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Air Force Health Study

*An Epidemiologic Investigation of
Health Effects in Air Force Personnel
Following Exposure to Herbicides*

MORTALITY UPDATE - 1991

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The purpose of the Air Force Health Study is to determine whether those individuals involved in the spraying of herbicides in Vietnam during the Ranch Hand operation have experienced any adverse health effects as a result of their participation in that program. The study is designed to evaluate both the mortality (death) and morbidity (disease) in these individuals over a 20-year period beginning in 1982.

The Baseline Mortality Report was released in June 1983, the Baseline Morbidity Report in February 1984. Follow-up mortality reports were released in 1984, 1985, 1986, and 1989. This study has not demonstrated health effects which can be conclusively attributed to herbicide or dioxin exposure.

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This report contains analyses of cumulative deaths occurring up to 31 December 1989. These data show no statistical difference between the cumulative mortality of 1,261 Ranch Hands and that expected based on a population of 19,080 Comparisons

The overall all-cause mortality experience of the Ranch Hands is not significantly different from that expected; 91 (7.2%) of the Ranch Hands have died; the expected number of deaths is 88.4. The overall observed and expected numbers of deaths were not significantly different for accidental deaths and suicides and for deaths caused by malignant neoplasm and heart disease. However, there were significantly increased Ranch Hand deaths due to digestive system diseases and, in nonflying enlisted personnel, circulatory system diseases. The increase in deaths caused by diseases of the digestive system has been previously noted is currently under investigation. The increased number of deaths due to circulatory system diseases among nonflying enlisted personnel is a new finding and is, as yet, unexplained.

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EXECUTIVE SUMMARY

An evaluation of cumulative all-cause Ranch Hand mortality through 31 December 1989 revealed no statistically significant difference between the observed and expected number of deaths (SMR=1.03, 95% CI 0.82-1.24, $p=0.79$). The indirectly standardized all-cause Ranch Hand death rate is 3.04 deaths per 1000 person-years; the Comparison rate is 2.95 deaths per 1000 person-years. Furthermore, the observed number of deaths is not statistically significantly different from the expected number in any of the subgroups of Ranch Hands determined by rank (officer, enlisted) and job (flyer, nonflyer).

Adjusted cause-specific analyses revealed no overall significant difference between the observed and expected numbers of deaths for accidental deaths (SMR=1.06), suicides (SMR=0.79), deaths due to malignant neoplasm (SMR=0.82), or deaths due to circulatory disease (SMR=1.14). However, there is a significant excess of deaths from circulatory disease among nonflying enlisted personnel (SMR=1.68, 95% CI 1.01-2.62, $p=0.02$).

There is a significant excess of Ranch Hand deaths caused by diseases of the digestive system (SMR=2.68, 95% CI 1.22-5.09, $p=0.005$). To date, 9 Ranch Hands have died of digestive diseases. These data could not be adjusted for alcohol use. Except for alcoholic cirrhosis of the liver and acute alcoholic hepatitis, the Ranch Hand deaths were caused by a variety of unrelated digestive system diseases. At the last analysis [5], there was also a significant excess of digestive disease deaths in Ranch Hands. At that time there were 6 deaths caused by digestive system disease (SMR=2.69, 95% CI 1.00-5.85, $p=0.01$).

The increased number of circulatory deaths in Ranch Hand nonflying enlisted personnel was not noted in the last report because previous reports incorporated a calculated dioxin exposure index. The index has since been found only weakly correlated with current or extrapolated dioxin body burden and has therefore been dropped from these mortality assessments. A reanalysis using 31 December 1987 as the cut point (as was used in the last mortality report) reveals a borderline significant increase in this stratum (SMR=1.59, 95% CI 0.79-2.40, $p=0.07$). Thus, the SMR for circulatory deaths has increased from 1.59 to 1.68 during the 2-year period from the end of 1987 to the end of 1989. This increase is of concern because Ranch Hand nonflying enlisted personnel have higher current dioxin levels than Ranch Hands in the other strata [7] and because current and extrapolated initial dioxin levels are significantly associated with diabetes and increased cholesterol, HDL cholesterol and triglyceride abnormalities. While there is no association

between dioxin and cardiovascular disease in the examined Ranch Hands, this increase in circulatory disease deaths could be dioxin-related through its association with diabetes and serum lipids. This possibility is being explored by review of the individual medical records of all Ranch Hands who have died of circulatory disease.

In summary, the overall all-cause mortality experience of the Ranch Hands is not significantly different from that expected. As of 31 December 1989, 91 (7.2%) of the Ranch Hands had died; the expected number of deaths is 88.4. The overall observed and expected numbers of deaths were not significantly different for accidental deaths, suicides, and deaths caused by malignant neoplasms or circulatory diseases. However, there were significantly increased Ranch Hand deaths due to digestive diseases and, in nonflying enlisted personnel, circulatory system diseases. The increase in deaths caused by diseases the digestive system has been previously noted is currently under investigation. The increased number of deaths due to circulatory system diseases among nonflying enlisted personnel is a new finding and is, as yet, unexplained.

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1. INTRODUCTION

This report updates the findings of prior Air Force Health Study mortality reports released in 1983 [1], 1984 [2], 1985 [3], 1986 [4], and 1989 [5]. The reader is referred to the baseline report [1] for information regarding the study design and the mortality determination process.

This report contrasts cumulative Ranch Hand mortality through 31 December 1989 (verified as of 15 March 1991) with that expected based on the mortality experience of the Comparison population of 19,080 Air Force veterans who flew or serviced C-130 cargo aircraft in Southeast Asia (SEA) during the same calendar period that the Ranch Hand unit was active in Vietnam.

Table 1 shows summary counts, person-years and death rates by group (Ranch Hand, Comparison). A person-year is the length of time lived by one person in one year. Persons surviving to the time of data analysis contribute the time, in years, between the dates of entry into follow-up and data analysis. Persons known to have died before the date of data analysis contribute the time, in years, between the dates of entry into follow-up and death. In this study, the date of entry into follow-up is the date of the start of duty in SEA. The date of data analysis is 31 December 1989. All analyses are based on regression analyses of the Standardized Mortality Ratio (SMR), the ratio of the observed to the expected number of deaths [6]. Because the statistical procedures produce inconsistent results when the expected number of deaths is small, a confidence interval and p-value are not provided when the expected number of deaths is less than 3. Expected deaths are additive across strata but not across different causes of death [6]. Except when otherwise noted, all death rates (per 1000 person-years), expected deaths and SMR's are adjusted for year of birth, rank (officer, enlisted) and military occupation in SEA (flyer, nonflyer).

In the hypothetical case that the Ranch Hand mortality experience is the same as that of the Comparisons, about 5% of the many statistical analyses shown in this report should be expected to produce p-values less than 0.05. The observation of significant results due to multiple testing on the same data, even when there is no group difference, is known as the multiple testing artifact and is common to all large studies. Hence, each significant result is scrutinized with regard to concomitant information to determine whether it can be reasonably attributed to herbicide exposure.

In all previous mortality assessments, a calculated dioxin exposure index was used to evaluate dose-response. Since the last mortality report [5], the index has been found to be only weakly correlated with actual dioxin body burden, expressed in parts per trillion (ppt), in Ranch Hands [7,8] and has therefore been dropped. Because none of the 91 dead Ranch Hands have been assayed for dioxin and 238 others have not been assayed or do not have a quantifiable result, the dioxin assay cannot be used to

assess dose-response patterns in the mortality data. The best indicators of dioxin exposure for mortality assessment are military rank and occupation in SEA. Of 932 living Ranch Hands who provided blood for dioxin testing, 866 had quantifiable dioxin levels and were fully compliant to the 1987 physical examination. The median dioxin level of those 866 was 12.8 ppt (range: 0-617.8). The median and range for flying officers (n=300), nonflying officers (n=19), flying enlisted personnel (n=148) and nonflying enlisted personnel (n=399) were 7.9 ppt (0-42.6), 6.7 ppt (3.1-24.9), 18.1 ppt (0-195.5) and 24.0 ppt (0-617.8). The median dioxin level of 804 Comparisons was 4.2 ppt and median dioxin levels among Comparisons did not vary significantly with rank or occupation.

At the last report, dates of military service in SEA for 8968 Comparisons were not available. Hence, dates for these Comparisons were randomly generated. In the interim, the service dates for 8937 of the 8968 were retrieved from military personnel records; the tour dates of 31 could not be verified due to missing records. Because their dates of service could not be verified, these 31 were declared ineligible and were excluded from the Comparison population. Additionally, one veteran previously included in the Comparison population was verified as ineligible and 11 veterans were newly verified as eligible Comparisons. The total number of Comparisons is now 19,080, 21 less than the 19,101 represented in the last mortality report.

The 31 Comparisons with missing personnel records are distributed by military occupation as follows: Nonblack flying officer; 1, Nonblack navigator; 3, Nonblack enlisted flight engineer; 3, Black enlisted flight engineer; 1, Nonblack nonflying enlisted personnel; 19, Black nonflying enlisted personnel; 4.

2. ALL-CAUSE MORTALITY

Summary mortality statistics for both populations are given in Table 1. In Table 1 and throughout this report, flying officers are pilots and navigators. Officers are flying officers and nonflying officers. Flying enlisted personnel are enlisted flight engineers. Nonflying enlisted personnel are enlisted ground personnel. Enlisted personnel are flying enlisted and nonflying enlisted personnel. All Ranch Hand death rates in Table 1 are adjusted via indirect standardization. Each indirectly standardized rate is the product of the Comparison death rate and the adjusted SMR (Table 3). The result is then multiplied by 1000 to give a death rate per 1000 person-years.

Table 1
Summary Counts and Adjusted Death Rates
By Rank and Occupation

Stratum	Ranch Hand				Comparison			
	At Risk	Dead	Person Years	Rate	At Risk	Dead	Person Years	Rate
Flying Officers	441	32	9555	3.37	5242	376	114858	3.27
Flying Enlisted	207	13	4503	2.45	2829	230	61059	3.77
All Flyers	648	45	14058	3.03	8071	606	175918	3.44
Nonflying Officers	26	2	562	3.50	284	20	6392	3.13
Nonflying Enlisted	587	44	12696	3.20	10725	615	238078	2.58
All Nonflyers	613	46	13256	3.19	11009	635	244470	2.60
All Officers	467	34	10118	3.40	5526	396	121250	3.27
All Enlisted	794	57	17199	2.91	13554	845	299137	2.82
Total	1261	91	27316	3.04	19080	1241	420388	2.95

Unadjusted occupation and race-specific mortality is summarized in Table 2. Some Ranch Hand death rates in Table 2 appear unusually high. For example, the Ranch Hand death rate among Black enlisted flight engineers is 12.52 deaths per 1000 person-years and the corresponding rate for all Comparison deaths in this stratum is 5.24 deaths per 1000 person-years. The four Ranch Hand deaths in this stratum have occurred since 1980. One of the 4 deaths was a suicide, 1 was accidental, 1 was due to a digestive system disease and 1 was due to ill-defined causes. An adjusted analysis shows that this increase is not statistically significant (SMR=2.23, 95% CI 0.61-5.71, p=0.100). In general, a death rate based on only a few deaths is not a reliable measure of mortality experience because one additional death can produce large changes in the death rate and in the SMR.

Table 2

Unadjusted Occupation and Race Specific Cumulative
All-Cause Mortality

a) Nonblack personnel

Stratum	Ranch Hand				Comparison			
	At Risk	Dead	Person Years	Rate	At Risk	Dead	Person Years	Rate
Pilots	351	25	7589	3.29	3417	270	74630	3.62
Navigators	82	7	1798	3.89	1773	105	39036	2.69
Nonflying Officers	25	2	541	3.70	280	20	6304	3.17
Flying Enlisted	192	9	4184	2.15	2606	205	56287	3.64
Nonflying Enlisted	534	40	11550	3.46	9689	541	215408	2.51
Total	1184	83	25662	3.23	17765	1141	391665	2.91

b) Black personnel

Stratum	Ranch Hand				Comparison			
	At Risk	Dead	Person Years	Rate	At Risk	Dead	Person Years	Rate
Pilots	6	0	127	0.00	20	1	452	2.21
Navigators	2	0	42	0.00	32	0	740	0.00
Nonflying Officers	1	0	21	0.00	4	0	88	0.00
Flying Enlisted	15	4	320	12.52	223	25	4772	5.24
Nonflying Enlisted	53	4	1146	3.49	1036	74	22670	3.26
Total	77	8	1656	4.83	1315	100	28722	3.48

Table 2 (Continued)

c) All personnel

Stratum	Ranch Hand				Comparison			
	At Risk	Dead	Person Years	Rate	At Risk	Dead	Person Years	Rate
Pilots	357	25	7716	3.24	3427	271	75082	3.61
Navigators	84	7	1840	3.80	1805	105	39776	2.64
Nonflying Officers	26	2	562	3.56	284	20	6392	3.13
Flying Enlisted	207	13	503	2.89	2829	230	61059	3.77
Nonflying Enlisted	587	44	12696	3.47	10725	615	238078	2.58
Total	1261	91	27316	3.33	19080	1241	420388	2.95

Survival analyses were carried out to assess Ranch Hand all-cause mortality with that expected relative to the Comparison population. All analyses were adjusted for rank (officer, enlisted), occupation (flying, ground) and date of birth in five-year intervals. The results are shown in Table 3. The expected numbers of deaths in Table 3 are sums of expected numbers of deaths within five-year intervals of year of birth. Each summand (not shown) is the product of the Ranch Hand person-years and the Comparison death rate.

Table 3

Adjusted All-Cause Standardized Mortality Ratios
by Rank and Military Occupation Among Ranch Hands

Stratum	Dead	Expected Deaths	SMR	95% C.I.	p-value
Flying Officers	32	31.07	1.03	0.67-1.39	0.87
Nonflying Officers	2	1.78	1.12		
All Officers	34	32.85	1.04	0.69-1.38	0.84
Flying Enlisted	13	20.00	0.65	0.35-1.11	0.12
Nonflying Enlisted	44	35.60	1.24	0.87-1.60	0.16
All Enlisted	57	55.60	1.03	0.76-1.30	0.85
All Flying Personnel	45	51.07	0.88	0.63-1.44	0.41
All Nonflying Personnel	46	37.38	1.23	0.87-1.59	0.16
All Ranch Hands	91	88.45	1.03	0.82-1.24	0.79

There are no overall differences between the observed and expected number of deaths from all causes in any stratum. The overall adjusted SMR for all Ranch Hands for all causes of death is 1.03, 95% CI 0.82-1.24, $p=0.79$.

Chi-square tests for trend were applied to all strata to assess the significance of trends in the SMR since 1985. These analyses were carried out twice, first with each of the years 1985 through 1989 separately contributing to the statistic and again with 1985 through 1987 collapsed to a single stratum and 1988 and 1989 collapsed to a second stratum. All analyses are conditioned on survival to 1 January 1985 and due to sparseness were not adjusted for date of birth. The tests are two-tailed and therefore would detect upward or downward trends in the SMR. Test results for detecting upward trends in the SMR may be derived from these results by dividing the p-value by 2 when the data indicate an increasing trend and replacing the p-value by 1.00 when the data indicate a decreasing trend. The results are shown in Table 4.

Table 4

Ranch Hand Mortality
Five-Year Trend Analysis

Flying Officers

One-Sample Chi-square(single year)=0.23 p=0.63
One-Sample Chi-square(85-87,88,89)=0.29 p=0.59

	Dead	Rate	Expected Deaths	SMR
1985	1	2.35	1.45	0.69
1986	5	11.84	1.79	2.80
1987	5	11.94	2.54	1.96
1988	5	12.11	2.69	1.86
1989	1	2.44	1.76	0.57

Enlisted Flyers

One-Sample Chi-square(single year)=0.11 p=0.74
One-Sample Chi-square(85-87,88,89)=0.10 p=0.75

	Dead	Rate	Expected Deaths	SMR
1985	1	5.07	0.89	1.12
1986	1	5.08	1.26	0.79
1987	1	5.11	0.82	1.22
1988	0	0.00	1.42	0.00
1989	1	5.13	0.75	1.34

All Flyers

One-Sample Chi-square(single year)=0.22 p=0.64
One-Sample Chi-square(85-87,88,89)=0.42 p=0.52

	Dead	Rate	Expected Deaths	SMR
1985	2	3.21	2.36	0.85
1986	6	9.70	3.09	1.94
1987	6	9.77	3.33	1.80
1988	5	8.22	4.12	1.21
1989	2	3.31	2.51	0.80

Table 4 (Continued)

Nonflying Officers

One-Sample Chi-square(single year)=2.93 p=0.09
 One-Sample Chi-square(85-87,88,89)=0.03 p=0.87

	Dead	Rate	Expected Deaths	SMR
1985	0	0.00	0.09	0.00
1986	0	0.00	0.18	0.00
1987	0	0.00	0.37	0.00
1988	0	0.00	0.37	0.00
1989	1	40.54	0.09	10.73

Nonflying Enlisted Personnel

One-Sample Chi-square(single year)=0.02 p=0.89
 One-Sample Chi-square(85-87,88,89)=0.17 p=0.68

	Dead	Rate	Expected Deaths	SMR
1985	2	3.59	2.16	0.93
1986	3	5.42	1.89	1.59
1987	2	3.63	2.37	0.84
1988	6	10.96	2.69	2.23
1989	1	1.84	2.47	0.41

All Nonflyers

One-Sample Chi-square(single year)=0.04 p=0.83
 One-Sample Chi-square(85-87,88,89)=0.19 p=0.66

	Dead	Rate	Expected Deaths	SMR
1985	2	3.44	2.26	0.89
1986	3	5.19	2.03	1.48
1987	2	3.47	2.63	0.76
1988	6	10.48	2.96	2.03
1989	2	3.52	2.57	0.78

Table 4 (Continued)

All Officers

One-Sample Chi-square(single year)=0.02 p=0.89
 One-Sample Chi-square(85-87,88,89)=0.32 p=0.57

	Dead	Rate	Expected Deaths	SMR
1985	1	2.22	1.54	0.65
1986	5	11.18	1.97	2.54
1987	5	11.27	2.90	1.73
1988	5	11.42	3.05	1.64
1989	2	4.60	1.86	1.08

All Enlisted Personnel

One-Sample Chi-square(single year)=0.07 p=0.79
 One-Sample Chi-square(85-87,88,89)=0.27 p=0.61

	Dead	Rate	Expected Deaths	SMR
1985	3	3.98	3.02	0.99
1986	4	5.33	3.02	1.32
1987	3	4.02	3.19	0.94
1988	6	8.08	4.00	1.50
1989	2	2.71	3.25	0.62

All Ranch Hands

One-Sample Chi-square(single year)=0.05 p=0.82
 One-Sample Chi-square(85-87,88,89)=0.57 p=0.45

	Number Dead	Rate Per 1000 Person Years	Expected Deaths	SMR
1985	4	3.32	4.63	0.86
1986	9	7.52	4.95	1.82
1987	8	6.72	5.86	1.36
1988	11	9.32	6.89	1.60
1989	4	3.41	5.12	0.78

The significant increasing trend in the SMR among flying officers noted in previous mortality reports is no longer present due to a decrease in the SMR since 1986. There are no apparent trends in the other strata.

A lexis diagram [9] for Ranch Hand flying officers is shown in Figure 1. Follow-up time is indicated for each living subject with a straight line beginning at his age and the beginning of his first qualifying tour of duty in SEA and ending with his age at 31 December 1989. Follow-up lines for deceased subjects end with a square at the subject's age at death and date of death. The corresponding diagram without the follow-up lines is shown in Figure 2. Lexis diagrams for nonflying officers, flying enlisted and nonflying enlisted personnel, without the follow-up lines, are shown in Figures 2 through 5.

Lexis diagrams provide another view of the data that permits a visual assessment of mortality clustering with respect to age and calendar time. A strong latency effect, for example, might be revealed by a cluster of deaths approximately 20 years after entry into follow-up. No such clusters are apparent in these data.

Figure 1
Lexis Diagram
Ranch Hand Flying Officers

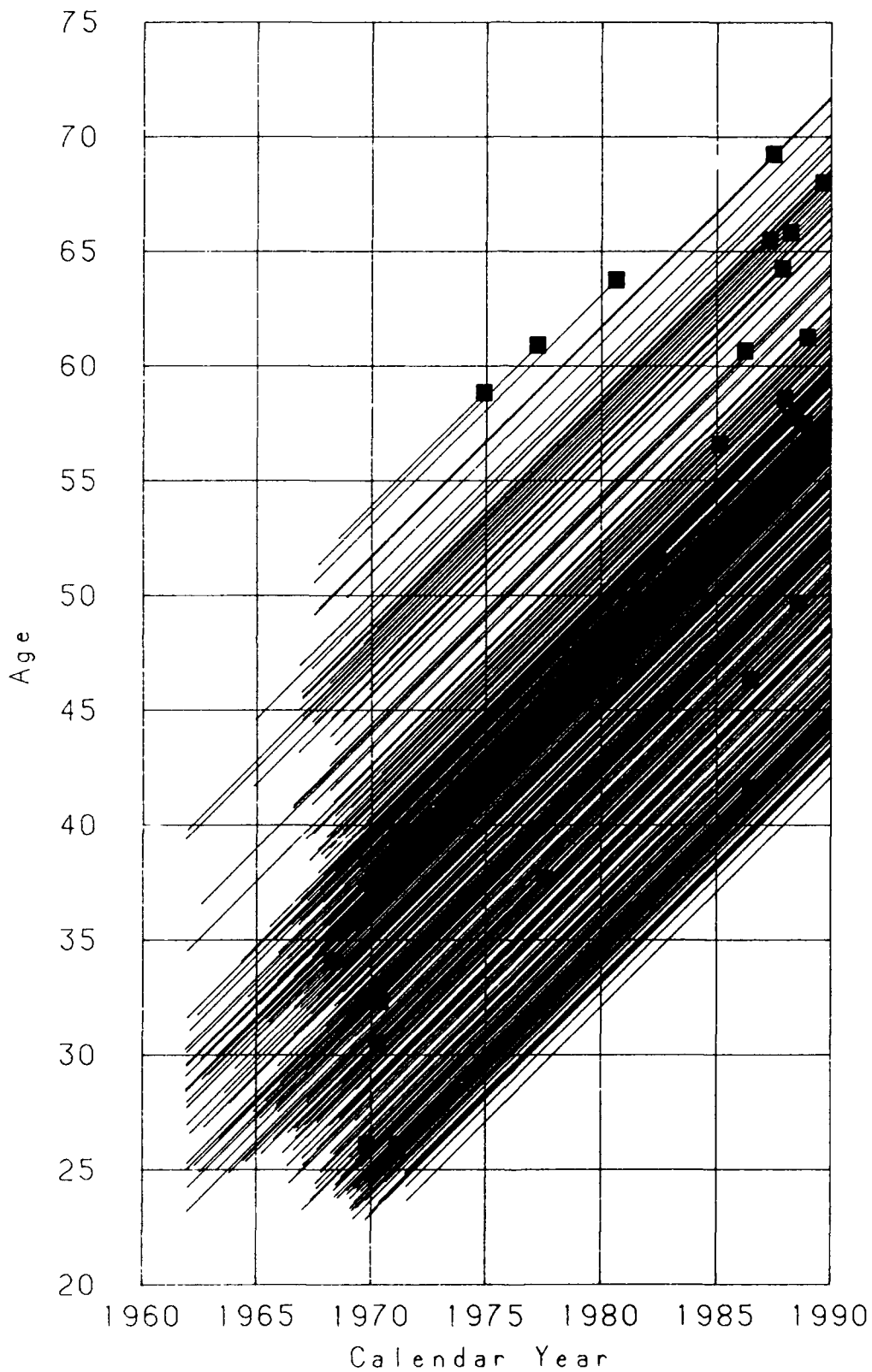


Figure 2
Lexis Diagram
Ranch Hand Flying Officers

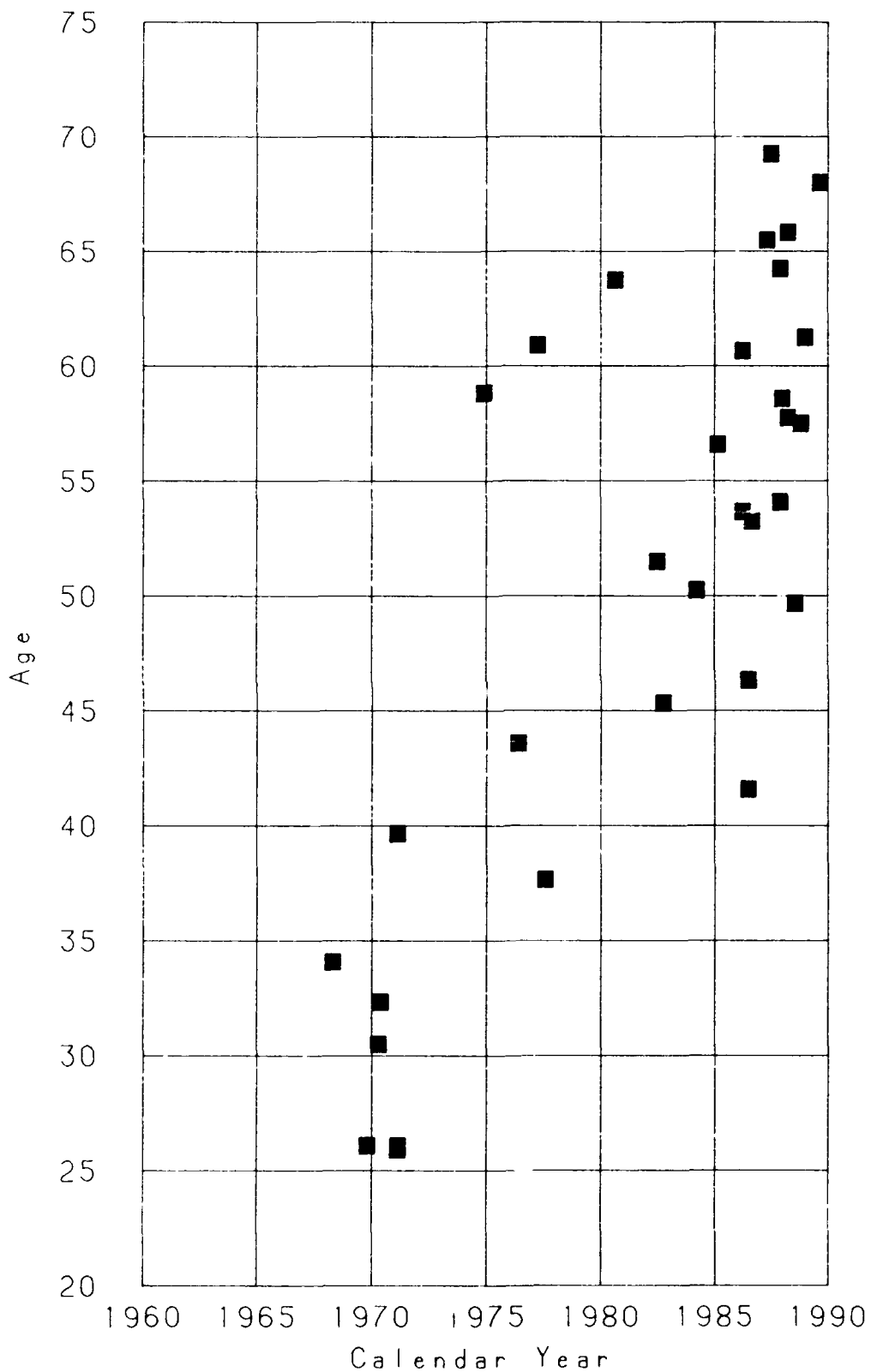


Figure 3
Lexis Diagram
Ranch Hand Nonflying Officers

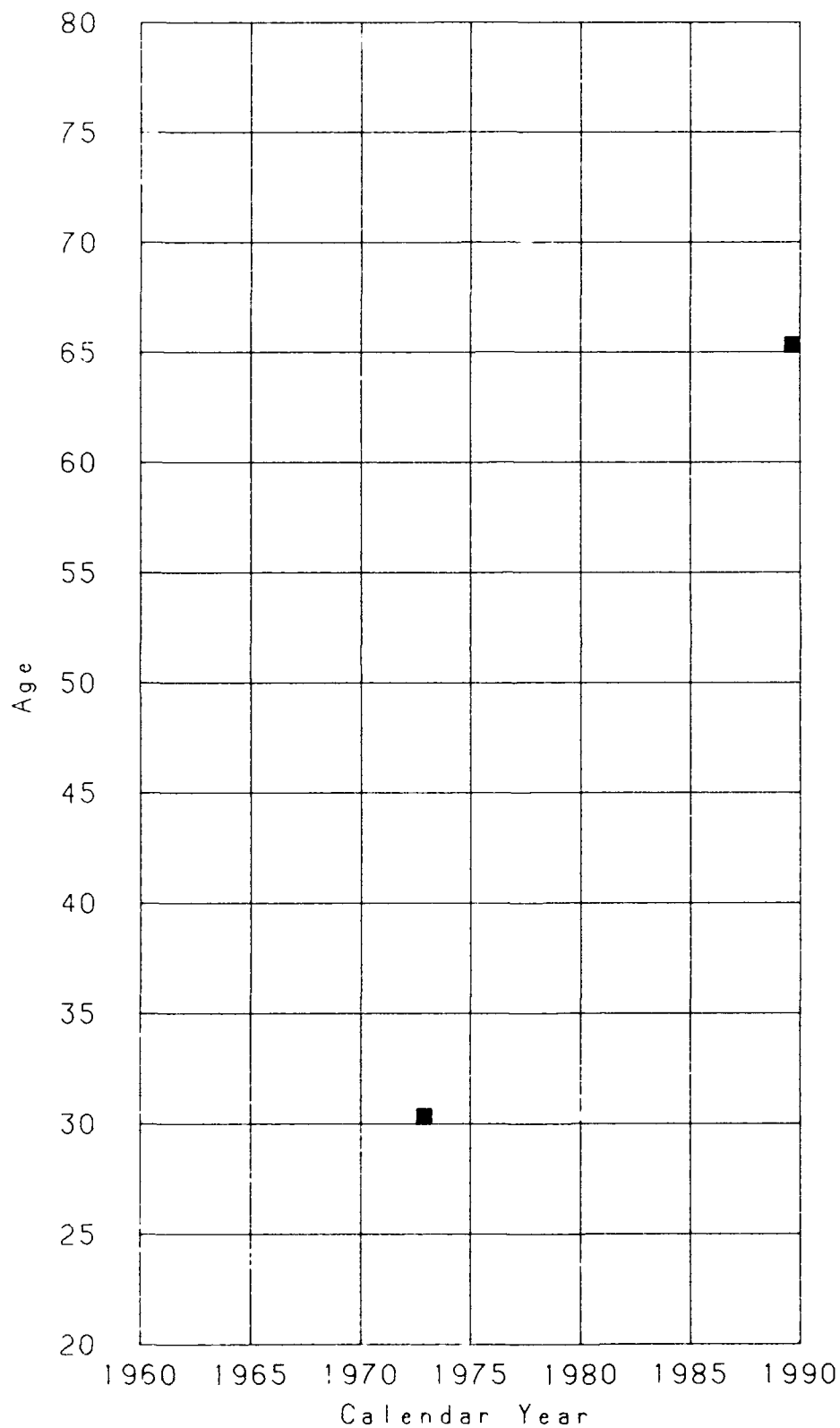


Figure 4
Lexis Diagram
Ranch Hand Flying Enlisted

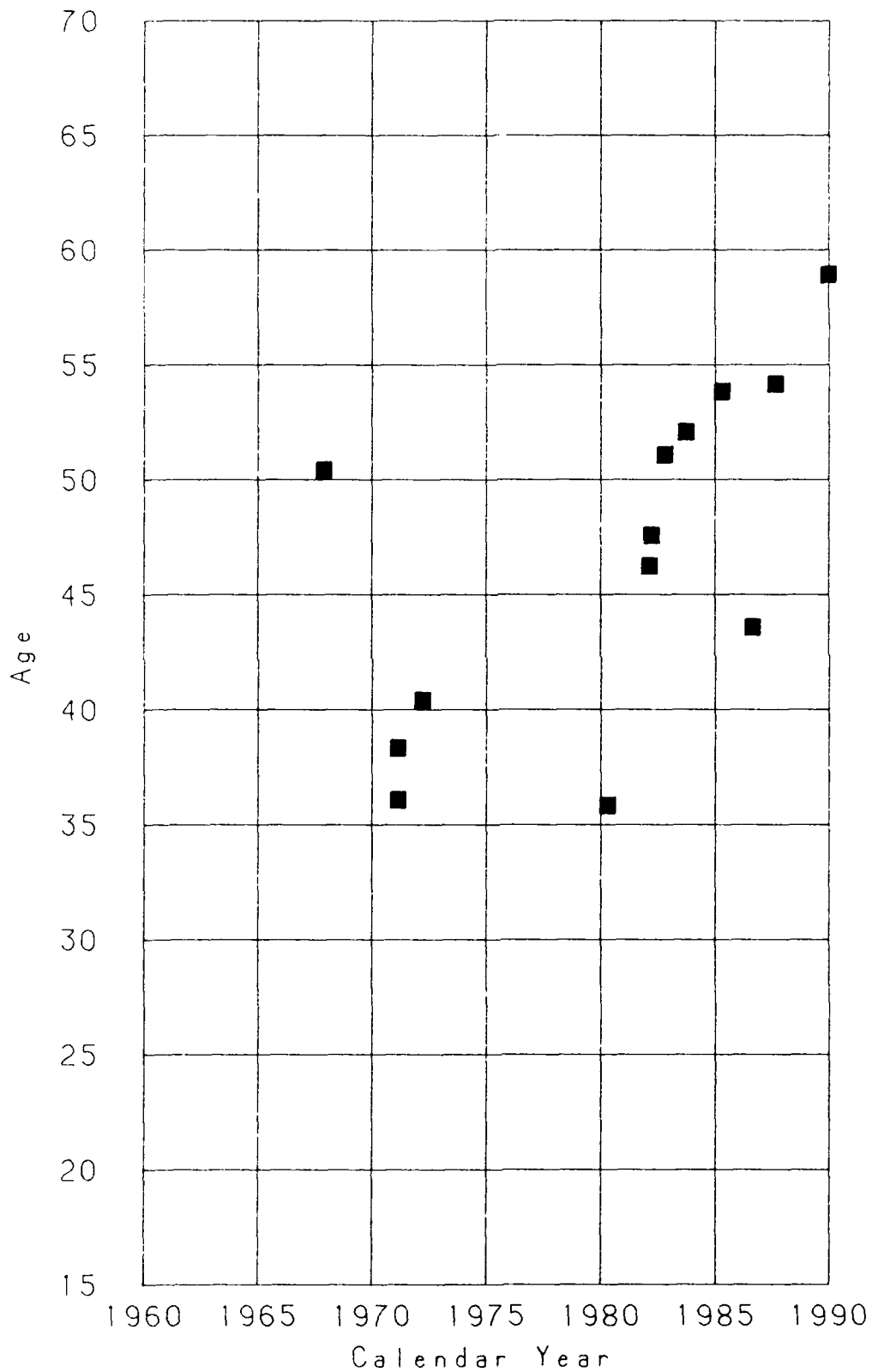
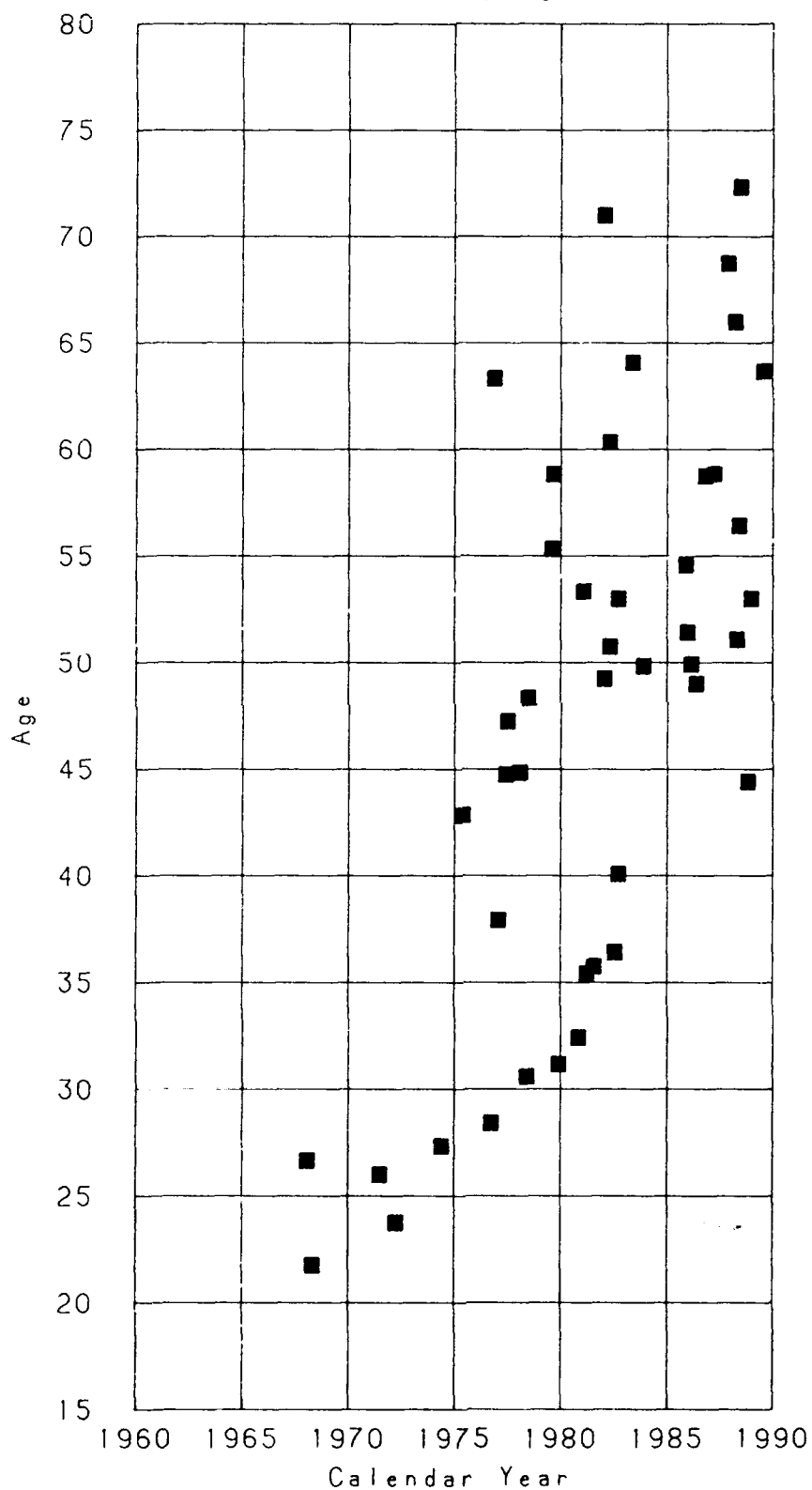


Figure 5
Lexis Diagram
Ranch Hand Nonflying Enlisted



3. CAUSE-SPECIFIC MORTALITY

Observed and adjusted expected Ranch Hand deaths by cause and stratum of rank and occupation are summarized in Table 5.

Table 5

Adjusted Cause-Specific Ranch Hand Mortality by Rank and Occupation

Cause	Stratum	Expected		SMR	95% CI	p-value
		Dead	Deaths			
Accidents	Flying officer	9	7.65	1.18	0.53-2.23	0.63
	Nonflying officer	0	0.10	0.00		
	Flying enlisted	4	5.32	0.75	0.21-1.92	0.57
	Nonflying enlisted	9	7.64	1.18		
	All Ranch Hands	22	20.71	1.06	0.62-1.51	0.78
Suicides	Flying officer	0	1.20	0.00	0.22-2.03	0.64
	Nonflying officer	1	0.12	8.64		
	Flying enlisted	2	1.34	1.49		
	Nonflying enlisted	1	2.38	0.42		
	All Ranch Hands	4	5.04	0.79		
Malignant Neoplasm	Flying officer	7	8.61	0.81	0.21-1.42	0.58
	Nonflying officer	1	0.58	1.73		
	Flying enlisted	1	4.39	0.23	0.50-2.06	0.81
	Nonflying enlisted	9	8.30	1.09		
	All Ranch Hands	18	21.88	0.82	0.44-1.20	0.41
Endocrine Disease	Flying officer	0	0.12	0.00		
	Nonflying officer	0	0.00			
	Flying enlisted	0	0.10	0.00		
	Nonflying enlisted	1	0.21	4.72		
	All Ranch Hands	1	0.43	2.32		
Circu- latory Disease	Flying officer	11	10.09	1.10	0.45-1.74	0.77
	Nonflying officer	0	0.78	0.00		
	Flying enlisted	2	5.98	0.33	0.04-1.21	0.15
	Nonflying enlisted	19	11.32	1.68		
	All Ranch Hands	32	28.17	1.14	0.74-1.53	0.47
Digestive Disease	Flying officer	4	1.01	3.95	1.22-5.09	0.005
	Nonflying officer	0	0.10	0.00		
	Flying enlisted	2	1.33	1.51		
	Nonflying enlisted	3	0.92	3.24		
	All Ranch Hands	9	3.36	2.68		

There are no overall or within-stratum significant differences between the observed and expected numbers of deaths due to accidents or malignant neoplasms (Table 5). One Ranch Hand died from endocrine disease (expected=0.1, SMR=3.32). There is also no significant difference between the observed and expected number of suicides in all Ranch Hands.

There is a significantly increased number of deaths caused by diseases of the circulatory system among Ranch Hand nonflying enlisted personnel (SMR=1.68, 95% CI 1.01-2.62, $p=0.02$) and significantly increased number of deaths due to digestive diseases in all Ranch Hands (SMR=2.68, 95% CI 1.22-5.09, $p=0.005$).

Additionally, 2 Ranch Hands were murdered (expected=1.60, SMR=1.25) and 3 died of unknown or ill-defined causes (expected=1.23, SMR=2.44).

Table 6 shows cumulative site-specific malignant neoplasm mortality among Ranch Hands.

Table 6

Site-specific Malignant Neoplasm Ranch Hand Mortality

Site	Dead	Expected Deaths
140-149 Lip, Oral Cavity and Pharynx		
140.9 Lip, Unspecified	0	0.060
141.9 Tongue, Unspecified	0	0.215
144.9 Floor of Mouth, Unspecified	0	0.057
145.3 Soft Palate	0	0.122
145.9 Mouth, Unspecified	0	0.111
146.0 Tonsil	0	0.143
147.9 Nasopharynx, Unspecified	0	0.102
148.1 Pyriform Sinus	0	0.178
149.0 Pharynx, Unspecified	0	0.115
150-159 Digestive Organs and Peritoneum		
150.3 Oesophagus, Upper Third	0	0.045
150.5 Oesophagus, Lower Third	0	0.070
150.9 Oesophagus, Unspecified	1	0.745
151.9 Stomach, Unspecified	1	0.395
153.4 Colon, Caecum	0	0.146
153.5 Colon, Appendix	0	0.109
153.6 Ascending Colon	0	0.045
153.9 Colon, Unspecified	0	2.019
154.0 Rectosigmoid Junction	0	0.098
154.1 Rectum	0	0.215
154.3 Anus, Unspecified	0	0.105
157.4 Islets of Langerhans	0	0.109
157.9 Pancreas, Unspecified	1	0.953
159.0 Intestinal Tract, Unspecified	0	0.058
160-165 Respiratory and Intrathoracic Organs		
160.9 Accessory Sinus, Unspecified	0	0.046
161.1 Supraglottis	0	0.109
161.9 Larynx, Unspecified	0	0.221
162.2 Main Bronchus	0	0.059
162.3 Upper Lobe, Bronchus or Lung	0	0.120
162.4 Middle Lobe, Bronchus or Lung	0	0.052
162.9 Bronchus and Lung, Unspecified	10	8.065
163.9 Pleura, Unspecified	0	0.055
164.9 Mediastinum, Unspecified	1	0.000
170-175 Bone, Connective Tissue, Skin and Breast		
170.9 Bone and Articular Cartilage, Unspecified	0	0.064
171.3 Connective, Soft Tissue, Lower Limb, Hip	1	0.000
171.8 Connective, Soft Tissue, Other	0	0.060
171.9 Site Unspecified	0	0.185
172.5 Skin, Trunk	0	0.063
172.9 Skin, Unspecified	0	0.649

Table 6 (Continued)

Site	Dead	Expected Deaths
179-189 Genitourinary Organs		
185.0 Prostate	0	0.224
188.9 Bladder, Unspecified	0	0.115
189.0 Kidney, Except Pelvis	1	0.436
190-199 Other and Unspecified Sites		
191.1 Brain, Frontal Lobe	0	0.112
191.4 Occipital Lobe	0	0.122
191.7 Brain Stem	0	0.103
191.9 Brain, Unspecified	1	0.694
195.0 Head, Face and Neck	0	0.271
195.8 Other Unspecified Site	0	0.058
197.0 Lung	0	0.059
197.5 Large Intestine and Rectum	0	0.061
199.0 Disseminated, Unspecified	0	0.068
199.1 Other, Unspecified	1	1.083
200-208 Lymphatic and Haematopoietic Tissue		
200.1 Lymphosarcoma	0	0.109
200.8 Reticulolymphosarcoma	0	0.102
201.9 Hodgkin's Disease, Unspecified	0	0.158
202.8 Other Lymphomas	0	0.455
203.0 Multiple Myeloma	0	0.401
204.0 Acute Lymphoid Leukaemia	0	0.051
204.1 Chronic Lymphoid Leukaemia	0	0.122
204.9 Lymphoid Leukaemia, Unspecified	0	0.079
205.0 Acute Myeloid Leukaemia	0	0.133
205.3 Myeloid Sarcoma	0	0.059
206.0 Acute Monocytoid Leukaemia	0	0.067
207.8 Lymphosarcoma Cell Leukaemia	0	0.060
208.0 Acute Leukaemia, Unspecified	0	0.185
Totals	18	19.497

The 18 Ranch Hand deaths due to malignant neoplasm do not appear to aggregate in an unusual pattern relative to that expected (Table 6).

The morphology of cumulative malignant neoplasm deaths is summarized in Table 7.

Table 7

Morphology of Ranch Hand Malignant Neoplasm Deaths

Morphology	Dead	Expected Deaths
M800 Neoplasms NOS		
140-149 Lip, Oral Cavity and Pharynx	0	0.053
150-159 Digestive Organs and Peritoneum	1	1.974
160-165 Respiratory and Intrathoracic Organs	4	3.437
179-189 Genitourinary Organs	0	0.232
190-199 Other and Unspecified Sites	1	1.005
239 Neoplasms of Unspecified Nature	0	
M801-M804 Epithelial Neoplasms NOS		
140-149 Lip, Oral Cavity and Pharynx	0	0.360
150-159 Digestive Organs and Peritoneum	1	1.370
160-165 Respiratory and Intrathoracic Organs	6	3.790
179-189 Genitourinary Organs	1	0.248
190-199 Other and Unspecified Sites	1	0.543
M805-M808 Papillary and Squamous Cell Neoplasms		
140-149 Lip, Oral Cavity and Pharynx	0	0.600
150-159 Digestive Organs and Peritoneum	0	0.073
160-165 Respiratory and Intrathoracic Organs	0	0.548
190-199 Other and Unspecified Sites	0	0.117
M814-M838 Adenomas and Adenocarcinomas		
140-149 Lip, Oral Cavity and Pharynx	0	
150-159 Digestive Organs and Peritoneum	1	1.627
160-165 Respiratory and Intrathoracic Organs	0	0.792
179-189 Genitourinary Organs	0	0.960
190-199 Other and Unspecified Sites	0	0.579
M856-M858 Complex Epithelial Neoplasms		
190-199 Other and Unspecified Sites	0	0.058
M872-M879 Naevi and Melanomas		
160-165 Respiratory and Intrathoracic Organs	1	0.000
170-175 Bone, Connective Tissue, Skin and Breast	0	0.712
M880 Soft Tissue Tumors & Sarcomas NOS		
170-175 Bone, Connective Tissue, Skin and Breast	0	0.121
190-199 Other and Unspecified Sites	0	0.052
M881-M883 Fibromatous Neoplasms		
170-175 Bone, Connective Tissue, Skin and Breast	1	0.000
M885-M888 Lipomatous Neoplasms		
170-175 Bone, Connective Tissue, Skin and Breast	0	0.064
M905 Mesothelial Neoplasms		
160-165 Respiratory and Intrathoracic Organs	0	0.113
M906-M909 Germ Cell Neoplasms		
190-199 Other and Unspecified Sites	0	0.064
M926 Miscellaneous Bone Tumors		

Table 7 (Continued)

Morphology	Dead	Expected Deaths
170-175 Bone, Connective Tissue, Skin and Breast	0	0.064
M938-M948 Gliomas		
190-199 Other and Unspecified Sites	0	0.852
M949-M952 Neuroepitheliomatous Neoplasms		
170-175 Bone, Connective Tissue, Skin and Breast	0	0.060
M959-M963 Lymphomas NOS or Diffuse		
200-208 Lymphatic and Haematopoietic Tissue	0	0.557
M964 Reticulosarcomas		
200-208 Lymphatic and Haematopoietic Tissue	0	0.109
M965-M966 Hodgkin's Disease		
200-208 Lymphatic and Haematopoietic Tissue	0	0.157
M973 Plasma Cell Tumors		
200-208 Lymphatic and Haematopoietic Tissue	0	0.401
M980 Leukaemia NOS		
200-208 Lymphatic and Haematopoietic Tissue	0	0.358
M982 Lymphoid Leukaemias		
200-208 Lymphatic and Haematopoietic Tissue	0	0.079
M985 Lymphosarcoma Cell Leukaemias		
200-208 Lymphatic and Haematopoietic Tissue	0	0.060
M986 Myeloid Leukaemias		
200-208 Lymphatic and Haematopoietic Tissue	0	0.113
M989 Monocytic Leukaemias		
200-208 Lymphatic and Haematopoietic Tissue	0	0.067
M990 Miscellaneous Leukaemias		
200-208 Lymphatic and Haematopoietic Tissue	0	0.059
Totals	18	21.878

Although the adjusted SMR for deaths due to malignant neoplasm is less than 1.0, there are morphologic subcategories of malignancies for which the SMR is greater than 1.0. For example, there are 9 Ranch Hand deaths from epithelial neoplasms not otherwise specified and the expected number of deaths in this category is 6.311. However, this excess is not significant (SMR=1.43, 95% C.I. 0.65-2.17, $p=0.28$).

4. CONCLUSIONS

An evaluation of cumulative all-cause Ranch Hand mortality through 31 December 1989 revealed no statistically significant difference between the observed and expected number of deaths (SMR=1.03, 95% CI 0.82-1.24, $p=0.79$). The indirectly standardized all-cause Ranch Hand death rate is 3.04 deaths per 1000 person-years; the Comparison rate is 2.95 deaths per 1000 person-years.

Furthermore, the observed number of deaths is not statistically significantly different from the expected number in any of the subgroups of Ranch Hands determined by rank (officer, enlisted) and job (flyer, nonflyer).

Adjusted cause-specific analyses revealed no overall significant difference between the observed and expected numbers of deaths for accidental deaths (SMR=1.06), suicides (SMR=0.79), deaths due to malignant neoplasm (SMR=0.82), or deaths due to circulatory system disease (SMR=1.14). However, there is an excess of deaths from circulatory system disease among nonflying enlisted personnel (SMR=1.68, 95% CI 1.01-2.62, $p=0.02$).

There is a significant excess of Ranch Hand deaths caused by diseases of the digestive system (SMR=2.68, 95% CI 1.22-5.09, $p=0.005$). To date, 9 Ranch Hands have died of digestive diseases. Except for alcoholic cirrhosis of the liver and acute alcoholic hepatitis, the Ranch Hand deaths were caused by a variety of unrelated digestive system diseases. At the last analysis [5], there was also a significant excess of Ranch Hand deaths caused by digestive diseases. At that time there were 6 Ranch Hand deaths caused by digestive system disease (SMR=2.69, 95% CI 1.00-5.85, $p=0.01$). This finding is currently under investigation.

These data could not be adjusted for alcohol use because alcohol consumption is known only for the 995 Ranch Hands and 1299 Comparisons who were fully compliant to the 1987 physical examination. Of the 91 deceased Ranch Hands and 1241 deceased Comparisons, 14 Ranch Hands and 19 Comparisons attended the 1987 physical examination. Thus, alcohol histories are unknown for 77 of the 91 deceased Ranch Hands and 1222 of the deceased Comparisons, as well as for 175 living Ranch Hands and 16,540 living Comparisons who were noncompliant to or ineligible for the 1987 physical examination.

A significant excess of deaths due to digestive system diseases in Army chemical corps veterans has been recently reported [10]. There was a 3-fold increase in digestive deaths in the chemical corps, primarily due to cirrhosis of the liver. Four of the 6 digestive deaths in chemical corps veterans were alcohol-related.

The increased number of deaths caused by circulatory system diseases in Ranch Hand nonflying enlisted personnel was not noted in the last report because previous reports incorporated a calculated dioxin exposure index. The index has since been found to be only weakly correlated with current or extrapolated dioxin body burden [7] and has therefore been dropped from these mortality assessments. A reanalysis using 31 December 1987 as the cut point (as was used in the last mortality report) reveals a borderline significant increase in this stratum (SMR=1.59, 95% CI 0.79-2.40, $p=0.07$). Thus, the SMR for circulatory deaths has increased from 1.59 to 1.68 during the 2-year period from the end of 1987 to the end of 1989. This increase is of concern because Ranch Hand nonflying enlisted personnel have higher current dioxin levels than Ranch Hands in the other strata [7] and because current and extrapolated initial dioxin levels are significantly associated with diabetes and increased cholesterol, HDL cholesterol and triglyceride abnormalities [7]. While there is no association between dioxin and cardiovascular disease in the examined Ranch Hands, this increase in circulatory disease deaths might be dioxin-related through its association with diabetes and serum lipids. However, only 1 Ranch Hand has died of circulatory system disease with mention of diabetes as contributory on the death certificate, versus 0.52 expected. The number of such deaths among all Ranch Hands is also 1 and the expected number is 1.04. Diabetes, as a secondary cause of death, is generally under-reported on death certificates. This limits the ability of this, or any other mortality study based on death certificates, to assess the possible relationship between dioxin exposure and mortality due to circulatory system diseases through an association between dioxin and diabetes.

In summary, the overall all-cause mortality experience of the Ranch Hands is not significantly different from that expected. As of 31 December 1989, 91 (7.2%) of the Ranch Hands have died; the expected number of deaths is 88.4. The overall observed and expected numbers of deaths were not significantly different for accidental deaths, suicides, and deaths caused by malignant neoplasms and circulatory system diseases. However, there were significantly increased Ranch Hand deaths due to digestive diseases and, in nonflying enlisted personnel, circulatory system diseases. The increase in deaths caused by diseases of the digestive system has been previously noted and is currently under investigation. The increased number of deaths due to circulatory system diseases among nonflying enlisted personnel is a new finding and is, as yet, unexplained.

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